UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,826	03/31/2004	Pamela J. Fereira	3139-6351.1US (ALZ5019/32	5280

24247 7590 11/10/2008

TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER	
FRAZIER, BARBARA S	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
11/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTOMail@traskbritt.com

Office Action Summary	Application No.	Applicant(s)	
	10/814,826	FEREIRA ET AL.	
	Examiner	Art Unit	
	BARBARA FRAZIER	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 17-31* is/are pending in the application.

4a) Of the above claim(s) *9,14 and 18-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-13,15 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-15 and 17-31 are pending in this application. Cancellation of claim 16 is acknowledged.

2. Claims 18-31 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/28/07.

3. Claims 9 and 14 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/28/07.

4. Claims 1-8, 10-13, 15, and 17 are examined.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. **Claims 1-8, 10-13, 15, and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 30-37 of copending Application No. 11/183,477.** Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same subject matter and composition components. Claim 30 of the '477 application is drawn to a stable non-aqueous drug formulation comprising a biocompatible polymer, a solvent, methionine, and a drug (compare instant claim 1). Claim 31 of the '477 application recites that the polymer is selected from the group comprising polyvinylpyrrolidone (compare instant claims 8 and 15). Claims 32 and 33 of the '477 application recite that less than about 35% of the drug is degraded by chemical pathways, and less than about 15% of the drug is degraded through aggregation (compare instant claims 2 and 3). Claim 34 of the '477 application is drawn to the drug formulation comprising particulate material (compare instant claim 4). Claims 35-37 of the '477 application are drawn to the drug formulation comprising medicines including the protein interferon (compare instant claims 5-7). Using the specification of the '477 application as a dictionary, the specification further defines the drug formulation as being single-phase (Title; compare instant claim 1), miscible in water (paragraph 30; compare instant claim 1), wherein the vehicle exhibits peroxide values below 5 ppm

(paragraph 32), having a viscosity in the range of about 1,000 to about 250,000 poise (paragraph 45; compare instant claim 10), comprising about 40% to about 80% polymer and about 20% to about 60% solvent (paragraph 46; compare instant claim 11), wherein the vehicle exhibits a moisture content of less than 5% (paragraph 49; compare instant claim 13), and wherein the biomolecular material (drug) is dispersed within the vehicle as a dry particulate material to create a suspension (paragraph 51; compare instant claims 12 and 17). Additionally, the formulation is defined as comprising omega interferon (paragraph 79), polyvinylpyrrolidone (claim 31), and benzyl alcohol (paragraph 44; compare claim 15 and the elected species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

7. Applicant's request that this provisional rejection be held in abeyance pending indication of allowable subject matter either in this application or in copending application 11/183,477 is noted. However, neither application has been allowed and both applications are currently still pending; therefore, the provisional rejection stands for reasons stated above.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. The previous rejection of claims 1-8, 10-13, and 15-17 under 35 U.S.C. § 112, first paragraph, is withdrawn in view of Applicant's arguments. However, claims 1-8, 10-13, 15, and 17 are newly rejected under 35 U.S.C. § 112, first paragraph in view of Applicant's amendment and for reasons set forth below.

10. **Claims 1-8, 10-13, 15, and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, as amended, now includes the limitation "wherein the polymer was treated with methionine in an amount sufficient to reduce vehicle peroxide values below 5 ppm (see lines 7 and 8 of claim 1). The only teaching in the specification of treating a polymer with methionine to reduce peroxide values is paragraph [0045], which teaches the removal of peroxides from PVP (polyvinylpyrrolidone) with 1% L-methionine solution, diafiltered using a Millipore TTF system to remove residual L-methionine, and lyophilized. The paragraph also states that PVP was processed to achieve peroxide values below 5 ppm. However, this disclosure does not teach how much methionine solution is used in order to achieve peroxide values below 5 ppm. Therefore, the specification does not provide a written description for the limitation "in an amount sufficient". Furthermore, the disclosure does not teach if other polymers can also be treated with methionine to achieve peroxide values below 5 ppm. Therefore, the

specification does not provide a written description for which polymers may be used as "the polymer" treated with methionine, other than PVP.

Claim Rejections - 35 USC § 103

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claims 1-8, 10-13, 15, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berry et al (WO 00/45790) and Chen et al (US 2003/018036), in combination alone or further in view of Kasraian et al (Pharm. Dev. And Tech., 4(4) 475-480, 1999) and Hunt (US 2003/0064536).

The claimed elected invention is drawn to a stable nonaqueous drug formulation comprising at least one drug; and a nonaqueous, single-phase vehicle comprising at least one polymer and at least one solvent, the vehicle being miscible in water, wherein the drug is insoluble in one or more vehicle components and the drug formulation is stable at 37 degrees C for at least two months, and wherein the polymer was treated with methionine in an amount sufficient to reduce vehicle peroxide values below 5 ppm (see claim 1). Applicants have elected the species wherein omega-interferon is the drug, polyvinylpyrrolidone is the polymer, and benzyl alcohol is the solvent.

Berry et al disclose stable non-aqueous single phase viscous vehicles and formulations comprising at least one beneficial agent uniformly suspended in the vehicle (abstract). The vehicle comprises polymer and solvent (page 6, lines 17-18) wherein the polymer is about 5% to about 30% and the solvent is about 30% to about 50% of the

vehicle (page 6, lines 20-22). The beneficial agent may be interferons (page 13, lines 29) and the polymer may be polyvinylpyrrolidone (page 12, line 18). The formulations may be stored at temperatures ranging from cold to body temperature (about 37 degrees C) for long periods of time (1 month to 1 year or more) (page 6, lines 27-30).

Berry et al do not specifically teach the use of benzyl alcohol as a solvent or omega-interferon as one of the interferons used as the beneficial agent. The formulation is also not taught as being miscible in water.

Chen et al teach catheter injectable depot compositions comprising polyvinylpyrrolidone polymer (paragraph 75) and benzyl alcohol solvent (paragraph 76); experimental data using the formulations made reveals that compositions comprising benzyl alcohol as the solvent show an improvement by reducing the injection force of the depot gel formulation (Examples 15 and 17). Chen et al also teach that omega-interferon may be used as the beneficial agent (paragraph 178), and that the compositions comprising polyvinylpyrrolidone and benzyl alcohol have a measure of miscibility in water (paragraph 21). Both the formulations of Berry et al. and the compositions of Chen et al. are drawn to compositions comprising interferon, polyvinylpyrrolidone, and solvent, to be used in drug delivery systems.

It is generally considered to be prima facie obvious to combine components each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from the being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of compositions for drug delivery systems. It therefore follows that the instant claims define prima facie obvious subject matter. Cf. In re Kerkhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Therefore, it would have been prima facie obvious at the time the invention was made to form a stable, nonaqueous composition by combining the interferon, polyvinylpyrrolidone and solvent of Berry et al. with the omega-interferon, polyvinylpyrrolidone and benzyl alcohol of Chen et al. in order to arrive at the claimed invention, with a reasonable expectation of success.

With respect to the drug being insoluble in one or more vehicle components (claim 1), Berry et al. teach that the beneficial agent is uniformly suspended in the vehicle (not solubilized), and thus would not be soluble in at least one of the vehicle components.

With respect to the polymer being treated with methionine in an amount sufficient to reduce vehicle peroxide values below 5 ppm, Berry et al do not specifically teach the treatment of the polymer with methionine to reduce the peroxide values of the formulation. However, Berry et al do teach that peroxides “not only adversely affect protein stability but would be toxic when delivered directly to, for example, the central nervous system of a human or animal” (page 4, lines 23-24). Therefore, one skilled in the art would assume that the peroxide values of the formulations made by Berry et al and Chen et al would also be less than 5 ppm, especially given the fact the components and use of the compositions of Berry et al. and Chen et al and the compositions of the claimed invention are the same.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

It is further noted that the limitation “the polymer was treated with methionine" is a product-by-process limitation. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. See MPEP 2113. In the instant claims, the limitation of treating the polymer with methionine to reduce peroxide values does not appear to impart a structural limitation to the formulation, other than the amount of peroxide values. Said amount would be obvious in light of the teachings of Berry et al (see page 8 of this action). Therefore, it appears that the process limitation of treating the polymer with methionine does not impart any additional structural limitation to the formulation other than what is already taught in the prior art.

However, should the process step of treating the polymer with methionine impart a structural limitation, the Examiner relies on the teachings of Kasraian et al and Hunt to demonstrate that said process step would be obvious to one of ordinary skill in the art.

Kasraian et al teach that polymers, such as PVP, often carry low levels of peroxides, which affect the stability of the product, as evidenced by color change. Control of the peroxides as trace impurities is suggested (see pages 476 and 477). The teachings of Kasraian et al are drawn to injectable formulations (see title).

Hunt teaches that peroxides can be reduced by inclusion of an amino acid which can act as an oxidative sink, that is as a scavenger for oxidizing compounds. A particularly preferred amino acid is methionine (see paragraph 117). The invention of Hunt is also drawn to injectable formulations (for example, see paragraph 141).

It would have been obvious to a person having ordinary skill in the art of injectable formulations to treat a polymer such as polyvinylpyrrolidone with methionine in order to reduce peroxide values below 5 ppm; thus arriving at the claimed invention. Kasraian et al fairly teaches that excipients such as PVP carry levels of peroxides, and Hunt fairly teaches that methionine reduces said levels of peroxides. Therefore, one skilled in the art would be motivated to treat the PVP to be used in a formulation with methionine in order to reduce peroxide value levels below 5 ppm. One would reasonably expect success from said process because the teachings of Kasraian et al and Hunt are both drawn to formulations suitable for delivering a drug, as are the inventions of Berry et al (page 7) and Chen et al (see abstract).

With respect to the amount and method of degradation of the drug (claims 2 and 3), Berry et al. does not specifically teach the percentage of drug degraded by chemical pathways or aggregation. However, Berry et al. do teach that the formulations maintain a high level of stability over time, wherein greater than 70% of the formulation is recovered at seven weeks (Tables 5 and 6). Based on this data, one skilled in the art would conclude that the level of degradation of the formulations would be comparable to that described in the claimed invention.

With respect to the drug being a particulate material (claim 4) that is dry (claim 12) and dispersed with the vehicle as a suspension (claim 17), Berry et al. teach that the active agent is buffered, then spray dried (page 16) before forming a uniform dispersion (page 17); Berry et al. also teach that drying the beneficial agent prior to formulation enhances the stability of the formulation (page 15).

With respect to the viscosity of the formulation (claim 10), Berry et al. describes the vehicle of the formulation as a "viscous vehicle", which means a viscosity that is preferably about 10,000 to 250,000 poise; this is encompassed by Applicant's viscosity of about 1,000 to about 250,000 poise.

With respect to the amounts of polymer and solvent (claim 11), Berry et al. disclose that the amount of the polymer is about 5% to about 30% and the amount of solvent is about 30% to about 50% of the vehicle (page 6, lines 20-22). This appears to be comparable to the amounts claimed by Applicants, especially given that the prior art uses the flexible modifier "about". In any case, it would have been obvious to determine workable and/or optimal amounts of polymer and solvent per the reasoning of well-established precedent, such as In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). (Holding that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.")

With respect to moisture content (claim 13), Berry et al. teach that the final moisture content of the viscous vehicle was less than 2% (page 15, line 2).

Response to Arguments

13. Applicant's arguments filed 7/25/08 have been fully considered but they are not persuasive.

Applicants argue that neither Berry et al nor Chen et al teach or suggest the newly added claim limitation that the recited polymer be treated with methionine in an amount sufficient to reduce vehicle peroxide values below 5 ppm.

This argument is not persuasive because the newly added limitation has now been addressed in the rejection, and is obvious for reasons stated above.

Applicants argue that the Office notes that neither Berry et al nor Chen et al teach or suggest anything about peroxide levels, so the claim limitation at issue would not be “obvious to try”.

This argument is not persuasive. Examiner disagrees with Applicant's assertion that the Office notes that neither Berry et al nor Chen et al teach or suggest anything about peroxide levels. On the contrary, Berry et al specifically teach that peroxides “not only adversely affect protein stability but would be toxic when delivered directly to, for example, the central nervous system of a human or animal” (page 4, lines 23-24). Therefore, one skilled in the art would assume that the peroxide values of the formulations made by Berry et al and Chen et al would also be less than 5 ppm, especially given the fact the components and use of the compositions of Berry et al. and Chen et al and the compositions of the claimed invention are the same.

Applicants finally argue that the cited references do not disclose each of the claim limitations in the pending claims, and accordingly a prima facie case of obviousness has not been made out by the Office.

This argument is not persuasive because Applicants do not distinctly point out which claim limitations are not disclosed in the cited references. Accordingly, it is the Examiner’s position that the claims are rendered obvious for reasons stated above.

Conclusion

No claims are allowed at this time.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611